radial distances were compared to those of the clinically used contours (inter-observer) and the average contours per patient and observer (intra-observer). The registration process was initiated with the localization of gold fiducial markers (FMs) and, if necessary, adjusted manually for rotation and/or translation. Prostate V100 and D90 were determined for each contour and registration. The two dosimetric parameters (DPs) were scaled with the patients clinical DPs (inter, see Figure 1) or the patients average per observer (intra) to remove the natural variation in DPs between patients.

Results: Prostate contours on US resulted in an inter-observer variability of 1.1 mm (1 SD with respect to the clinical contours) and an intra-observer variability of 0.6 mm (1 SD with respect to the average contour per patient and observer). US-contouring alone led to dosimetric differences of 1.6% of the clinical V100 and 9.3% of the clinical D90, and an intra-observer variability of 0.6% (V100) and 1.0% (D90).

US-CBCT registrations varied within 2.0% of the clinical V100 and 3.1% of the clinical D90. For MRI-CBCT registration, this was 1.3% and 2.1% respectively. The intra-observer variabilities of US-CBCT (V100: 0.9% and D90: 1.5%) and MRI-CBCT (V100: 0.7% and D90: 1.0%) registration were smaller than the inter-observer variabilities. During registration, observers found 91% of the FMs on US, 100% on CBCT and 99% on MRI. 78% of the US-CBCT registrations were manually adjusted based on the urethra contours and iodine seeds. MRI-CBCT registrations were manually adjusted in 18% of the studies.

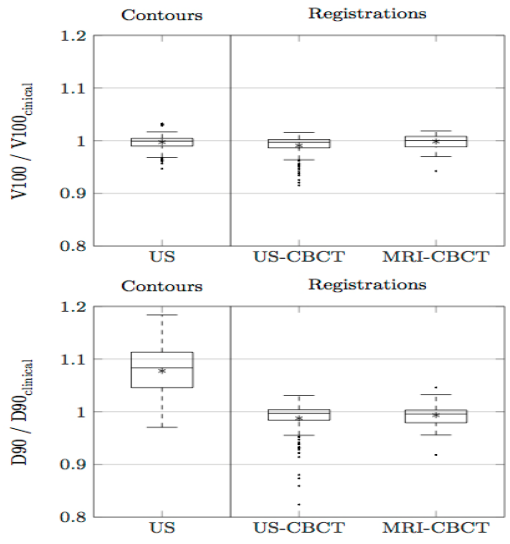

Figure 1: V100 (top) and D90 (bottom), scaled by the respective clinical parameters, originating from observer contours on US and US– and MRI–CBCT registrations. The symbol (∗) is displayed at the observer mean.

Conclusions: US- and MRI-CBCT registrations showed little variability compared to the inter-observer variability in US-contouring. Inter-observer contouring caused D90 variations of 9.3% from the clinical value. The intra-observer contouring variability was comparable to the registration variability.

Good FM visibility on MRI scans resulted in small registration variabilities. The inferior FM visibility on US was compensated by the manual adjustment based on seeds and urethra.

OC-0087

HDR brachytherapy combined with interstitial hyperthermia for prostate cancer - tolerance and toxicity

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Purpose/Objective: Evaluation of tolerance, early and late toxicity of HDR brachytherapy combined with interstitial hyperthermia (IHT) in patients treated for prostate cancer.

Materials and Methods: 105 patients were treated for prostate cancer using HDRBT combined with IHT. 79 patients were treated fo primary prostate adenocarcinoma, and 26 patients for local recurrence after previous definitive EBRT. The treatment of 76 patients consisted of external beam radiotherapy (EBRT) to the total dose of 50 Gy and HDRBT boost (21Gy in 2 fractions), 3 patients received HDRBT as a monotherapy to the total dose of 45 Gy in 3 fractions. Salvage HDRBT for local cancer recurrence was performed to the total dose of 30 Gy in 3 fractions. IHT was planned before each HDRBT fraction to the temperature of 40-43ºC for 60 minutes. Toxicity was assessed according to Common Toxicity Criteria for Adverse Events version 4.03.

Results: The median follow-up time was 26.4 months (range 7 - 61 months). We didn't observe any grade 3 or higher gastrointestinal (GI) or genitourinary (GU) early toxicities. Early GU grade 1 and 2 toxicities were common, but only two patients (1,9%) experienced acute urethral stenosis and required temporary catheterisation (grade 2). Only two patients (1,9%) developed late grade 3 urinary tract obstruction with urinary retention, which required transurethral resection of the prostate (TURP). The incidence of grade 2 toxicity in this group of patients did not exceed 30%. There were no late grade 2 or higher complications from the gastrointestinal tract. There were no statistically significant differences in early complications between the groups of patients treated with radical and salvage intent, except for haematuria ($p < 0.01$) and rectal bleeding ($p < 0.01$).

Conclusions: The combination of HDRBT with IHT is well tolerated. The profile of early and late complications is acceptable, while the incidence of grade 3 toxicity remained within a few percent only.

OC-0088

Evaluation of dose-predictors of urethral strictures for prostate patients treated with HDR brachytherapy

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Purpose/Objective: High Dose-Rate brachytherapy (HDRB) for the treatment of prostate cancer provides biochemical control comparable to other treatment modalities with the benefit of reducing dose to the OARs. Generally delivered in conjunction with external beam radiotherapy HDRB has the potential advantage of allowing dose escalation due to the high dose delivered during the treatment fraction. However, the wide ranges of fractionation regimes used in different centres make it difficult to establish clear guidelines for

organs-at-risk toxicity. This study was performed to assess the best dosimetric predictor of urethra strictures.

Materials and Methods: Patients treated between 2001 and 2013 at a single institution with HDRB were retrospectively analysed. The patients were all reviewed 6, 12, 18, 24 months and then every year until 10 years after the treatment and data collected in a database. Clinical, demographic, dosimetric and urethral stricture factors were captured. We used urethra Dose Volume Histograms (DVH) metrics: D10% (Gy), D5%(Gy) and D30%(Gy). We converted doses from 3 different fractionation regimes (18 Gy in 3, 19 Gy in 2 and 18 Gy in 2 fractions) into Biological Effective Dose (BED) with α/β = 5 Gy. Univariate and Multivariate logistic regression were used to evaluate factors predictive of urethral stricture after HDRB.

Results:

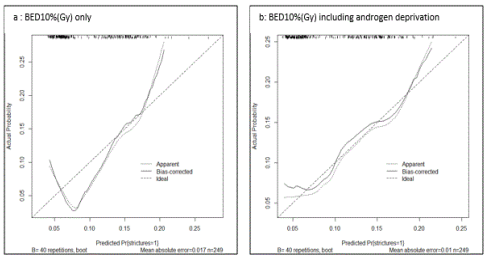

Figure 1: Calibration curves obtained with BED10% (Gy) (a) and BED10% (Gy) associated to neoadjuvant androgen deprivation (b).

We analysed data from 249 patients, with a median follow-up of 7 years (1.4- 13.4 years). Urethra strictures were present in 25/249 (10%) patients, and the median time to onset stricture was about 1.5 years (1 month-7 years).

On univariate analysis, BED10%(Gy) (OR = 1.05, p= 0.01), BED30%(Gy) (OR = 1.05, p= 0.02), and BED5%(Gy) (OR=1.05, p= 0.01) were significantly correlated to urethra stricture. The AUC of the resulting model was 0.62 in all cases, however calibration was always suboptimal. Calibration showed improvement when the dosimetric factors were associated to clinical factors despite their lower significance, such as use of neoadjuvant androgen deprivation (OR=0.5, protective factor) which was present in 232 patients (Figure 1).

Conclusions: Urethra DVH metrics are related to stricture, particularly the dose to small urethra volumes (D10%). However androgen deprivation acts as an important dose response modifier, pointing out the importance of integrating dosimetric and clinical information in order to have a better identification of the subgroup of patients at high risk of developing severe urinary toxicity after HDRB.

OC-0089

Phase II trial of dose escalation to dominant intraprostatic lesion with TRUS-MRI guided real time HDR brachytherapy

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Purpose/Objective: To demonstrate the feasibility, safety and effectiveness of dose escalation to Dominant Intraprostatic Lesion (DIL) as defined on multiparametric MRI (mpMRI) with Real-Time MRI-TRUS fusion High-Dose-Rate (HDR) Brachytherapy

Materials and Methods: 15 patients with intermediate-high risk Prostate cancer and visible dominant intra-prostatic nodule on mpMRI have been treated prospectively. The treatment consisted of combined MRI-TRUS fusion HDR-brachytherapy (1 fraction of 1500 cGy) and Hypofractionated external beam (3750 cGy in 15 fractions) (BED: 265Gy).

Prostate gland, DILs and Organs at risk (OARs) were delineated on MRI dataset, MRI-TRUS fusion performed and contoured structures transferred to the US dataset.

The homogeneity parameters used for optimization aim were prostate-V100 > 98%, V150 of 25-33%, V200 < 8%, urethral Dmax < 115% and rectal D1cc < 70% of prescribed dose. Within these constraints, a dose of 1875 Gy was delivered to at least 98% of the DIL volume (V125%>98%)(BED: 351Gy)

Results: Median age was 70 years, median prostate volume was 23.8 cc, median number of needles was 16 (13-18). Dose escalation to DIL was feasible in 14/15 patients (93%) without violating dosimetric constraints and 1 patient presented a minimal deviation of dosimetric restrictions. Median prostate V100, V150 and V200 were 98.2, 30.6 and 7.4% respectively. Median urethral Dmax was 114.1%, median rectal D1cc was 62.8%. Median V100, V125, V150 and V200 to DIL were: 100, 99, 78.5 and 20% respectively.

With a median follow-up of 10 months (range 9-16), none of the patients developed acute urinary retention, only 2 patients presented acute GU grade 2 toxicity, none of the patients developed chronic grade ≥2 toxicity. All patients returned to the pre-treatment IPSS level after 2 months of follow-up.

In addition to standard PSA follow-up, response has been assessed by mpMRI at 12 months. All patients evaluated with MRI presented a complete response based on functional parameters.

Conclusions: This study demonstrates that dose escalation to DIL with MRI/TRUS fusion guided HDR brachytherapy is feasible, longer follow-up will demonstrate the safety and efficacy of this procedure.

OC-0090

Salvage HDR-brachytherapy for previously irradiated locally recurrent prostate cancer

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Purpose/Objective: External Beam Radiotherapy (EBRT) is considered the standard practice for localized prostate cancer. Although this, local relapses are not negligible and the ideal salvage treatment is not well-defined. We report our outcomes in terms of efficacy and safety of Salvage High-Dose-Rate Brachytherapy (HDRB) for locally recurrent prostate cancer after definitive radiation therapy (RT).

Materials and Methods: From august 2004 to July 2014 we retrospectively analyzed 60 patients (pts) undergoing HDR-BT after pathologic confirmation of locally recurrent disease. The median age at recurrence was 66 years (55-77) and, the median PSA was 4'13ng/ml (1'27-17). Gleason score and T scale were 7 and T2, respectively. Prescribed total dose was 38Gy. Pts received 4 fractions of 9'5Gy with 2 implants separated 2 weeks. The 6% of pts received neoadjuvant hormonotherapy and, 11% received adjuvant hormonal